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Original Articles, Selections and Translations.

ART. I.—ON THE ANATOMICAL AND PHYSIOLOGICAL EFFECTS OF STRYCHNIA ON THE BRAIN, SPINAL CORD AND NERVES.

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IT is with considerable misgiving that I undertake to describe anatomical changes produced in the nervous system of the economy by the drug strychnia. Many have tried, but thus far in vain, to discover some effect that they could state positively was produced by strychnia. The trouble is, that pathological changes are met with, but it is hard to tell if they are simply post-mortem, or if they are produced by strychnia. While an ordinary practitioner should be able to determine with the microscope the various kinds of abnormal growths, yet it requires years devoted to the one subject, with constant practice, to recognize any changes produced in nerve substance itself. Again, the effects of the various reagents used in preparing the specimens may mislead one, and make him think he sees things he does not see. So, altogether, the subject is fraught with difficulties; and I will be only too much pleased if I can succeed in throwing even the shadow of a light on the obscure problem. I claim, at least, that the sections were prepared with the utmost care; that all parts of the nervous system have been examined, and examined closely; and that, in *every case*, sections have been made of both the normal tissue and the strychnized tissue, taken from precisely the same spot in two different animals, and the two carefully *compared.*

As just stated, in each case two rabbits were used, both in good health, one of which was killed by cutting the medulla spinalis between the occiput and the atlas, and the other killed by hypodermic injections of strychniæ acetas in the leg.

Post-mortem examination with the naked eye in the strychnized rabbits showed excessive congestion. So great was this that, in one instance, on showing to a friend the specimens I had obtained, and which I had suspended in a bottle, he said, "How did you inject these specimens?"—so certain was he that I *had* injected them; and this ran throughout the whole brain and cord, and was not confined to the membranes; indeed, the latter had been removed in the case mentioned above.

On removing the skull-cap and the processes of the vertebræ, the sight was really sickening. I can express it by no other word; and the astonishing thing is that the animal could have lived as long as it did—great swollen vessels standing out, gorged, and looking, under the microscope, like twisted cords, the blood with difficulty held in by the thin walls of the small arteries and capillaries, and threatening to break through its investments.

Of change in the nerve substance proper, I have little to say.

(1) The sciatics were used to examine the effects of the drug on the *nerves* in their course, being carefully teazed out. The cells themselves showed no change whatever in any case, the normal and the strychnized specimens side by side having the same appearance. The only thing noted was a change, real or apparent, in the axis cylinder. It came out more distinctly in the normal than in the strychnized specimen. The white substance of Schwann appeared perfectly normal.

(2) The brain proper showed no great lesion, except that in the grey substance there was apparently granular disintegration, in some places quite general, and in others, here and there,

in little spots. This, too, was apparent in the cord, extending into the white substance. This is all that could be noted in any case. The question now arises, Is this simply a post-mortem change, or is it due to the strychnia? I think it is a *secondary* result of the strychnia, due to the intense vascular engorgement. This is justifiable, because both the normal and the poisoned nerve were treated in every way the same, both in respect to time, and condition, and the reagents in which they were placed; so that they ought to have had the same appearance if the strychnia had not produced any effect. At the same time, I do not think this is a primary change, due to the strychnia, but a secondary one, due probably to the vascular changes, and that, if there were another drug producing the same effects physiologically, it would also produce the same anatomical changes. To any one who has examined the brain and cord of an animal killed by strychnia, the vascular changes are seen to be sufficient to cause death. The nerve-cells throughout the brain and cord are squeezed and pushed, and their functions must be disturbed; the relations of the blood and the cephalo-rachidian fluid fluctuate violently. Many of the symptoms are the same as in compression of the human brain. This fact seems to have escaped notice hitherto. The pupil is widely dilated, the pulse is slowed, there is vaso-motor paralysis, yet the temperature is little changed in either case. And now, in addition to all these sufficient causes of death, no one seems to have remembered (that I am aware of) that the *respiratory centre* is affected; that the granular disintegration that has been noticed occurs. I propose to show hereafter that this little spot is more especially affected, and through it, of course, the respiratory and cardiac movements. The vascular engorgement of the rest of the nervous substance would tend to produce paralysis, but not necessarily death; while the vascular engorgement of this little tract would produce certain death, unless the action of the lungs and heart were kept up by artificial means.* This explanation accords exactly with the physiological action of the drug, as detailed below. I think I prove conclusively that the nerves in their course are not affected by this drug, and so we find few changes. Now, this

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*Vide page 648, *et seq.*

is as it should be, for the nerves in their course do not suffer the compression that the brain and cord do; in fact we might disregard the infinitesimal quantity, and say they do not suffer at all. The paralysis all over the body is purely spinal; the nerves themselves respond perfectly to any stimulation. So, to my mind, this explanation is conclusive, and I do not think we need or ought to look for further changes in the nerve substance than would be produced by the vascular engorgement, remembering the symptom of compression of the human brain, and the great effect this engorgement has on the respiratory and cardiac centres.

I.

It would be a work of supererogation for me to enumerate the great physiologists who have experimented on the action of strychnia. The conditions of this paper do not require it. I trust I may be pardoned, however, if I call to mind the names of Majendie in 1809, Stannius in 1837, and Van Deen in 1839. Then follows the noble work of the lamented M. Claude Bernard, and M. Brown-Séquard's experiments, begun in 1849, and continued at intervals ever since. In 1858 Koelliker published his experiments, and in 1860 Martin-Magron and Buisson published their interesting paper in Brown-Séquard's *Journal de la Physiologie.* Then follows Vulpian, and many others—names that it would be a pleasure to write did time and space permit.

With regard to the action of strychnia on the motor nerves, I must be more explicit, as the results have apparently been so heterogeneous in nature. MM. Mueller, Matteucci, Moreau, Ambrosoli, Wittich and Martin-Magron and Buisson asserting that the poison effectually paralyzes the motor nerves, while MM. Bernard, Koelliker, Pelikan, Valentin, and Vulpian, in quite as positive a manner, assert that it does not act on the motor nerves in their course, or influence them in the least after once leaving the spinal cord. We will shortly narrate (in their proper sequence) some experiments that we hope will tend to clear up these doubts, and place the matter in a way of being definitely settled.

I will now narrate some of my own experiments on the nervous system. The strychnia that I used was prepared by Messrs. Powers & Weightman, of Philadelphia. The ordinary tests were applied, and it was found to be *perfectly pure.* In each cubic centimetre of distilled water there was dissolved by the aid of acetic acid, one hundredth of a gramme of strychnia, and the solution gave a neutral reaction with litmus paper. For the purpose of electric irritation, I made use of one Grove cell, eighty millimetres high, and fifty-five millimetres in diameter. I also used DuBois Reymond's induction apparatus, with Helmholtz's modification for equalizing the opening and closing currents, in connection with DuBois' key. The induction apparatus was graduated by means of a scale, marking the fractions of centimetres, 0 representing the condition of the apparatus when the secondary coil was pushed completely over the primary coil, hence representing the strongest position of the apparatus.

From the salient phenomena of poisoning by strychnia, so well known to all, we are justified in assuming that the alkaloid exerts its peculiar power either on the cerebrum, on the efferent nerves, on the afferent nerves, or on the gray matter of the spinal cord. We will consider each in turn. Before proceeding to examine these points *seriatim*, however, let me narrate a few experiments I have made in connection with the general action of the alkaloids on guinea-pigs, pigeons, turtles and snakes.

Guinea Pig. At 4:00 P. M., .005 gramme of the acetate of strychnia was injected hypodermically into the leg. At 4:1 short, rapid breathing and trembling. At 4:2:30 rolls over in a general and severe convulsion. At 4:3:30 sensation increased; tetanus continues. At 4:4 retches; frequent but short convulsions. At 4:7 dead. Chest opened at 4:14; ventricles beat 26 per minute; auricles beat 50 per minute. Autopsy—Intense congestion of all the organs; right ventricle full of blood, but left ventricle empty.

Pigeon. At 3:58 P. M. received .0025 gramme of strychnia hypodermically in the leg. At 3:59 excessive tetanus. At 4:00 tetanus frequent and prolonged. At 4:1 no cessation; 4:2:15 dead. At 4:13 the sciatic nerve responded with the coil marking 0.

Snake. At 1:15 P. M. the cord was cut below the medulla oblongata, and .01 gramme of strychnia was injected into the lower segment of the body. Rapid tetanus of an exquisite character occurred. As the poison gradually coursed down the spine, the tetanoid phenomena were manifested at different points of the body. Sometimes a space of a foot in length would form a firm arch, standing upright on the table.

Vulpian says that he has produced an effect by introducing strychnia under the skin of an earth-worm, but that it was merely local. On crabs it has hardly any action. He introduced as much as ten centigrammes of strychnia, sometimes into the tissues, and sometimes into the lungs, without producing the least toxic effect.*

I procured a turtle, and injected as much as a tenth of a gramme. No characteristic phenomena of poisoning were produced. On opening the turtle the next day, its heart was found still beating.

But to return. We are to consider whether strychnia exerts its peculiar power on the cerebrum, on the afferent nerves, on the efferent nerves, or on the grey matter of the spinal cord. That the convulsions are not cerebral is shown by the following experiment, one of fifteen that I performed in this connection: The encephalon was removed by cutting through the medulla spinalis, on a line with the posterior edge of the tympana. The convulsions not only occur, but they are much more violent after cutting the cord, because we remove the influence of the centre for the inhibition of reflex action, situated, according to Setschenow, in the corpora quadrigemina and thalami optici.

Frog. Weight 13 grammes. At 3:7 P. M. receives .005 gramme of strychnia, injected into the lungs. At 3:7:30 general tetanus ensues. At 3:11 the cord was cut, but prolonged tetanus remained until 3:21:30, when the frog was dead.

Frog. Weight 14 grammes. At 3:18 P. M. .005 gramme of strychnia was injected into the lungs. At 3:18:15 general tetanus ensues. At 3:20 ablation of the cerebrum. The tetanus continued unabated till 3:25, when the observation was

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***Leçons sur la Physiologie*, etc., page 448.

suspended. That the poison does not affect the peripheral terminations of the sensory or motor nerves, may be seen, as in the following experiments, seven in number, of which I relate two as examples: I cut off the access of the poison entirely from one leg, by tying all the arteries and veins on that side. In spite of this operation, the convulsions took place with as great force as if it had not been performed.

Frog. Weight 20 grammes. Right iliac artery and veins tied. At 11:13 A. M. .005 gramme of strychnia was injected into the lungs. Hops away. At 11:15 general tetanus, and opisthotonos at 11:15:30. The convulsions show no preference for any part of the body, being as strongly marked in the right leg as anywhere else. At 11:16 the same phenomena show themselves. At 11:17 the rigidity is so great that the frog can be made to stand up on either hind leg. At 11:19 the muscles of the right side of the body are hard and tense, the gastrocnemius standing out prominently. At 11:35 dead.

Frog. Weight 22 grammes. Right iliac artery and veins tied. .005 gramme of strychnia is injected into the lungs at 11.48 A. M. At 11:50 convulsions. At 11:53 spontaneous tetanus all over the body, including the right leg. At 12:1 the tetanus is almost as marked in the right leg as anywhere else in the body. At 12:15 dead.

In order to determine whether the poison could affect either the sensory or motor nerves during their course, after leaving the spinal cord, I cut the cord below the origin of the brachial plexus, but left all the nerves going to the posterior extremities intact. I then severed all the spinal branches of the aorta below the point of section, and on administering strychnia, I found that no tetanus whatever occurred, there was no hyperæsthesia (that is to say, no more than would be due to the removal of Setschenow's centre), but perfectly normal reflex action remained. The minutiæ of two of these experiments (six in number) are detailed as follows:

Frog. Weight 20 grammes. Medulla spinalis cut below the origin of the nerves of anterior extremities, and the spinal branches of the aorta severed. At 11:31 A. M. .005 gramme of strychnia was injected into the lungs. At 11:32 great irritability was shown in the fore part of the body, but none in the posterior extremities. At 11:33 tetanus in front, but no movement of the hind legs. Indeed, tetanus did not occur at any time in the hind legs. The frog was dead at 12:10 P. M.

Frog. Weight 25 grammes. Cord cut below the brachial plexus, and spinal branches of the aorta severed. At 12:11 P. M. .005 gramme of strychnia was injected into the lungs. At 12:12 heightened sensibility in front legs and head, but only normal reflex action in hind legs. At 12:14 violent convulsions in upper part of the body, but not even a tremor in the hind legs, the quadriceps flexors and gastrocnemii soft and flaccid. At 12:16 the tetanus became so violent in the fore part of the body, that it lasted continuously for two minutes, the eyes being closed and sunken in the head, and the head itself twisted violently backwards, but the hind legs remained unaffected. At 12:25, dead.

The experiments that I now relate prove conclusively that the grey matter of the spinal cord must be the seat of the tetanus-producing action of strychnia. In these cases the poison was cut off from the posterior extremities, but was allowed free access to the spinal cord, and, as a result, general tetanus was induced. I made five experiments under this head, of which I relate two as examples:

Frog. Weight 67 grammes. The aorta was tied above its bifurcation, and at 6:44 P. M. .005 gramme of strychnia was injected under the skin of the lower jaw. At 6:46 tetanus occurs over the whole body, without discrimination. At 6:48 the cord was cut, but general tetanus still continues, till, at 7:15, the animal dies.

Green Frog. Weight 103 grammes. Aorta tied above its bifurcation. At 12:13 P. M. .005 gramme of strychnia was injected under the skin of the back. At 12:17, general tetanus occurred over the whole body. At 12:18, emprosthotonos. General convulsions occurred till the observation was suspended.

The question has been agitated for some time as to whether the motor nerves are paralyzed in poisoning with strychnia. Many eminent names are arrayed on each side, as shown above, and it is difficult to explain how it happens that such contrary results could be obtained as those at present on record. At first I thought that perhaps the difficulty lay in the species of frogs, as some experimenters used the *Rana temporaria*, and some the *Rana esculenta*; but I procured animals of both these species, and have obtained exactly the same results in each. Perhaps it was due to the means of irritation, as many of them used Pulvermacher's apparatus, which is by no means constant, or, perhaps, the nerves were not handled carefully enough, and thus sustained a traumatic injury in dissecting them. Again, if the nerve was raised on a thread, the irritation might have been applied to the proximal and not to the distal end. But these are only surmises. Should any of them be true, the fault doubtless must be laid to an oversight on the part of the experimenters, and not to a positive error. Again (and this, perhaps, is the more likely), the strychnia may not have been pure. Few, if any, of these observers mention having tested their strychnia, I believe. Now, we all know that the strychnia of commerce contains more or less *brucia*, and this may paralyze the motor nerves, though strychnia does not. I have instituted a series of experiments with *brucia*, which may yield an explanation of this difference of results. Many are the charges that have been brought against those who asserted the non-paralyzation of the motor nerves. It has been said that they did not give large enough doses of the poison, or that they tested the nerves too soon. But both of these charges must be unfounded, as I have given as much as one-tenth of a gramme (1.54 grains) to a frog weighing only eighteen and a half grammes, and have tested the sciatic an hour after the animal was dead and the heart ceased beating, and have found it still capable of responding. Great care was observed in the following experiments, that the current should not spread to the muscle, by raising the nerve high up on a silk thread. The strength of the current was also accurately noted by means of DuBois' graded coil, with which a platinum zinc cell was used. To determine this point I have made thirty-seven (37) experiments, of which I relate a few. The notes of all the others, which are before me, exactly accord with these. In each case the frog was weighed, so that a comparison might be made between the weight of the frog and the amount of the strychnia injected.

Green Frog. Weight 120 grammes. At 11:50 A. M. .005 gramme of strychnia was injected into the lungs. At 12:30 .01 gramme more was injected; same dose repeated at 12:32, and again at 12:34. Some time after the heart had ceased beating the sciatic was irritable. At 2:15 the left sciatic responded at 11 centimetres of DuBois' coil, and at 2:52 it did the same. At 2:55 the right sciatic responded at 13 centimetres, and again at 4:18 with the same strength of the current. At 4:18 the left sciatic responded at 11 centimetres. At 6:17 the left responded at 11 centimetres, and the right sciatic at 8.5 centimetres.

Frog. Weight 15 grammes. At 4:48 P. M. .01 gramme of strychnia was injected under the skin of the lower jaw. At 4:48:30 general tetanus. At 4:53, both sciatics irritable at the weakest current. At 5:00, dead—both sciatics respond to the weakest current. At 5:30 both sciatics respond to 4 centimetres.

Frog. Weight 14 grammes. At 10:44 A. M. received .05 gramme of strychnia into the lungs. At 10:44:30 tetanus. At 10:52 dead. At 10:53 the sciatics respond at 14.5 centimetres, DuBois' coil. At 11:53 the sciatic responds at 15 centimetres. At 11:20, sciatic nerve responds at 7 centimetres. At 11:30, sciatic responds with secondary coil pushed over primary coil. At 12 M. the same phenomena.

Frog. Weight 18.5 grammes. At 10:49 A. M. 1 gramme of strychnia was injected into the lungs. At 10:49:10, tetanus. At 10:58, heart stopped. At 10:59, sciatic responds at 14.5 centimetres. At 11:02, the same. At 11:19, sciatic responds at 7 centimetres. At 11:30, sciatic responds with secondary coil pushed over primary coil. At 11:52 and 12 M. the same phenomena were observed.

On the authority of the large number, and the universally constant results of these experiments, I think we are not presumptuous in asserting our conviction that strychnia does not paralyze the motor nerves. It must be remembered that if a galvanic irritation is applied too frequently, the neurility of a nerve will be destroyed, and you will fail to elicit a response, independently of any poison. This, too, may be another reason that so many experimenters have decided the converse of our proposition.

Dr. Sigmund Mayer,* Assistant to the Physiological Institute at Prague, and Dr. Wilhelm Schlesinger, are the only two who have given us any definite information as to the effects of strychnia on the blood-pressure. Mayer used the nitrate, having dissolved .0008 grm. in every cubic centimetre of distilled water. He always gave tinct. opii before operating. He gave two cubic centimetres of his solution by means of the jugular vein, and noticed in thirty seconds a rise in the pressure, and a more frequent pulse. He reasoned that the rise was due, either to the opposition to the blood current, produced by contraction of the muscles, or else to the action of the carbonic acid on the nerve centres in the heart. He thinks that it is not due to any action of the muscles, nor to any "besoin de respirer," because he obtained the same results with animals rendered quiet by curare, and while using artificial respiration. But no change in the pulse was produced under these circumstances, hence the pressure and pulse are mutually independent. In very large doses the pressure did not rise. The rise, therefore, is due to an irritation of the vaso-motor centre, and a consequent contraction of the arteries. In large doses the vaso-motor centre is paralyzed. He says that after cutting the cord, either no rise, or only a very small one took place. Irritation of the cut ends of the crural nerves, produced a marked rise, according to the force of the current, from which he reasons that the ganglia between the sensory and vaso-motor nerves are not altered.

The pulse he found inconstant: if the pneumogastrics were cut, the pulse was not slowed. The pulse sometimes rose in connection with the tetanus, especially in non-curarized animals. He says that strychnia not only can excite the vaso-motor centre, but also the origin of the inhibitory fibres of the pneumogastrics. He finally concludes that the slowing of the pulse is only due to a want of oxygen, which reacts on the central ends of the pneumogastrics, for he could not obtain it if he used artificial respiration, though the pressure still remained far above normal. Hering* thinks that the quickening of the pulse, where it occurs, is due to apnœa (apnoë) produced by the frequent inspirations.

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* *Stricker's Jahrb.*, 1872, 111.

Dr. Schlesinger† published his article in 1874, in which he agrees with Mayer as to some of the main points above related. He says the rise in pressure is not due solely to the influence of a vaso-motor centre, situated in the medulla oblongata, but in a great measure is due to vaso-motor centres in the spinal cord, at present only determined for strychnia. On cutting the cervical cord, as is acknowledged by all, the pressure falls, but on exhibiting strychnia, a considerable rise in the blood-pressure is called forth. This rise, he says, both absolutely and relatively, exceeds the rise with the cord intact. Irritation which, after separation of the brain from the cord, no longer exerts an influence on the blood-pressure, after the injection of strychnia causes a marked rise. This result holds good for curarized animals, in whom the sympathetics and pneumogastrics have been cut. On consulting his results, I find that the highest rise he obtained was from fifteen millimetres, after cutting the cord, to one hundred and fifty millimetres after injecting strychnia, and the lowest rise was from twenty to fifty. He made all his experiments on rabbits, and used either the crural or the sciatic nerve for the purpose of irritation. He concludes that, first, vaso-motor centres exist below the fourth ventricle (*Rautengrube*) for strychnia at least, which the latter throws into inordinate action, whereas, otherwise they are quiet; second, strychnia by arrest of the respiration, in most cases shows a rise in pressure; third, on irritating a spinal nerve, a rise in pressure is induced, after cutting the cord.

I will now relate some of my own experiments with regard to the influence of strychnia on the nerves that govern the circulatory system. Upon warm-blooded animals, these amounted to twenty-three in number, of which I only detail two or three under each division. I used the same solution as before, namely, .01 gramme of the poison, dissolved in one cubic centimetre of distilled water, with the aid of acetic acid, the solution being absolutely neutral. I also used DuBois-Reymond's induction apparatus, with Helmholtz's modification, for the purpose of irritation, as described above. In order to maintain artificial respiration, an apparatus was employed on the principle of Springel's blower. A metronome, attached to a Grove battery, by breaking and renewing the current at regular intervals caused a weight to fall on the tubing, thus imitating normal rhythmic respiration. The pulse and pressure were noted on the drum of Ludwig's registering apparatus, which was connected with his mercurial manometer. Throughout the tubing of the manometer, a saturated solution of bi-carbonate of soda was passed to keep the blood from clotting. The time was registered by means of a pen, connected with an electro-magnet; to this was joined Bowditch's clock, which, by breaking and renewing the current every second, caused the pen to inscribe the latter interval of time upon the drum. The strychnia was injected by means of a canula, placed in the external jugular vein, to which a hypodermic syringe accurately fitted. Great care was observed that no air entered the vein. The poison was in all cases injected toward the heart. The kymographion was connected to the external carotid artery by means of a canula bound in the artery. As the tetanic convulsions would influence the circulation, curare was used in just sufficient quantity to prevent any muscular movements.

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* *Stricker's Jahrbuecher* for 1872.

† *Stricker's Jahrbuecher*, 1874, page 20.

Ex.—*Rabbit*, curarized. Tracheotomy; canula in right jugular. Carotid used for observation. *All nerves intact.* Artificial respiration, &c.

TIME.	PULSE.	PRESSURE.
9:48:0	76	133
.01 gram. strychnia injected.		
9:48:15	44	154
9:48:30	21	128
9:48:45	27	120
9:49:0	34	152
9:49:45	30	122
9:50:45	36	126
9:53:0	47	130
9:54:15	50	136
10:0:0	33	91

I omitted saying above that I have made twenty-three (23) successful experiments with warm-blooded animals (rabbits, cats, and dogs) on the nerves governing the circulatory system.

TIME.	PULSE.	PRESSURE.
10:5:15	36	89
10:9:15	34	100
.005 gram. strychniæ acetas injected.		
10:9:30	37	96
10:10:0	44	52
10:11:15	46	70
10:17:0	47	76
10:20:38	44	64
Observation suspended.		

Ex.—*Cat*, curarized. Tracheotomy; canula in left jugular; carotid used for observation. *All nerves intact;* artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
12:26:45	52	86
.005 gram. strychniæ acetas injected.		
12:27:0	51	86
12:27:15	49	86
12:27:30	51	148
12:27:45	49	144
12:28:0	49	128
12:28:15	49	107
12:28:30	48	96
12:28:45	48	90
12:29:0	47	86
12:29:15	46	86
12:29:45	47	86
12:39:45	46	80
.005 gramme of strychniæ acetas injected.		
12:40:0	47	80
12:40:15	47	84
12:40:30	47	94.5
12 41:0	46	91
12:57:15	44	66
12:58:0	43	64
.01 gram. strychniæ acetas injected.		
12:58:15	36	59
12:58:30	36	50
12:59:0	30	40
1:0:0	25	23
1:4:0	26	36
1:5:0	25	38
1:25:0	21	27
1:29:45	14	20
Observation suspended.		

These experiments are simply given as examples. All the others are in perfect accord with them. They show that the general action of strychnia is to slow the pulse, and, by irritating the vaso-motor centre, to cause a contraction of the capillaries and small arteries, and thus to increase the arterial pressure. Following this irritation, if small doses are given there is a steady fall in pressure, until the animal dies (if the dose has been a lethal one). If large doses are given, there is a primary paralysis of the vaso-motor centre or centres, and the pressure constantly falls immediately. The fall in pressure cannot be due to a weakened heart, since strychnia does not affect the muscular system, as proved by Vulpian* and confirmed by many experiments that I myself have made. To what is the decrease of the pulse frequency, then, due? It

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may be due either (*a*) to a central, or (*b*) to a peripheral stimulation of the pneumogastrics, or (*c*) to action on the excito-motor ganglia of the heart itself. It will be remarked that sometimes, on injecting the poison, the pressure does not rise, or rises only very slightly after having given several doses previously. This, I think, is due to the fact that the nerve centres have lost, to a great degree, their power of responding. The animal's heart still beats, but practically it is dead.

In order to determine whether the phenomena above stated were due to a central stimulation of the vagi, I cut both these nerves in the neck, thus entirely removing their central action, but leaving their peripheral action free to exercise its power.

Large rabbit, curarized. Tracheotomy; canula in right jugular; carotid used for observation. *Both vagi cut*; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
12:00	67	120
.005 gram. strychniæ acetas injected.		
12:0:15	63	145
12:0:30	46	200
1:0:45	50	182
12:1:15	50	170
12:2:4	60	160
12:3:15	47	100
A clot occurring in the carotid canula, some time was consumed in removing it.		
12:23:15	44	82
12:23:42	44	76
12:25:12	47	90
.005 gramme strychnia injected.		
12:25:30	46	89
12:25:45	44	74
12:26:0	46	39
12:26:15	34	32
12:26:45	34	26
12:27:15	32	26
12:27:30	30	26
12:28:30	30	26
Observation suspended.		

Little kitten, curarized. *Both pneumogastrics cut in neck;* tracheotomy; artificial respiration; canula in left jugular; carotid used for observation.

TIME.	PULSE.	PRESSURE.
5:6:15	54	118
.0025 gramme strychnia injected.		
5:6:30	53	98
5:6:45	46	69
5:7:0	22	48
5:7:15	17	44
5:7:30	31	38
5:7:45	29	37
5:8:0	28	34
5:8:15	26	30
5:10:15	17	16
5:10:30	16	14
5:10:45	15	14
5:11:0	14	12
Observation suspended.		

The same result as to both pulse and pressure follows; hence strychnia does not decrease the pulse through central stimulation of the vagi. Now, it is well known that atropia has the power of paralyzing the ganglia at the peripheral ends of the pneumogastrics, and thus removing their inhibitory action on the heart. I administered a solution of the sulphate of atropia by means of the jugular vein, in just sufficient quantity to effect this paralysis. To determine when I had attained this result, I applied a strong induction current to the course of the pneumogastrics. When these had no effect on the cardiac action, it was evidence of the paralysis of these ganglia.

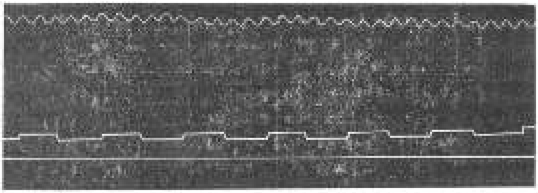
Rabbit. Canula in left jugular; carotid used for observation; pneumogastrics paralyzed by atropia, as tested by strong currents; curare; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
5:32:0	74	108
.00125 gramme strychnia injected.		
5:32:15	55	126
5:32:30	54	124
5:33:0	54	120
5:33:30	54	117
5:34:0	52	112
5:34:30	50	108
5:35:0	53	102
5:36:0	53	102
5:37:0	54	100
5:38:0	53	101
5:39:0	47	94
.00125 gramme strychnia injected.		
5:39:15	43	88
5:39:45	45	80
5:40:30	44	70
5:41:30	46	72
5:42:30	45	74
Observation suspended.		

Rabbit. Canula in left jugular; carotid used for observation; pneumogastrics paralyzed by atropia, as tested by strong currents; curare; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
4:45:30	59	80
.0025 gramme strychnia injected.		
4:45:45	57	92
4:46:0	51	94
4:46:30	51	94
4:47:15	47	82
4:48:0	49	75
4:49:0	48	78
4:50:0	49	78
4:51:30	51	83
.0025 gramme strychnia injected.		
4:51:45	50	74
4:52:0	46	50
4:53:0	44	46
4:53:45	45	58
4:54:30	45	60
4:56:0	47	70
4:59:30	47	78
.0025 gramme strychnia injected.		
4:59:45	46	64
5:0:0	41	44
5:1:0	42	46
5:2:15	42	54
5:11:15	41	50
5:15:0	41	45
5:18:0	38	36
Observation suspended.		

These experiments show that strychnia does not exert its influence through any stimulation of the regulator ganglia. Therefore, by a process of exclusion, negatively, it must affect the excito-motor ganglia of the heart. I now propose to prove this positively in the case of mammals, and later, also, in the case of frogs. I cut the pneumogastrics, the sympathetics and the depressor nerves of Ludwig, in the neck, and placed the heart beyond the control of the acceleraotrs and the vaso-motor centre in the medulla oblongata, by severing the spinal cord just below the medulla. It will be observed that the pulse is slowed steadily; hence, I think, proving conclusively that the seat of the decreased pulse-frequency is in the ganglia of the heart.



NOTE.—It may not be amiss for me to state the mode in which these results were recorded on the drum, and the method pursued in counting them. In order to do this the more clearly, I insert a specimen of one of the tracings. The drum is covered with smoked paper, and, when the experiment is finished, this paper is cut off and passed through a simple varnish made of shellac and alcohol in proper proportions. The broken line is that which was recorded by the pen which marked the time, each break denoting one second. The straight line is the abscissa, and the highest line, of course, marks both the pulse and the arterial tension. The mode of procedure is to mark off a certain number of seconds; then to erect ordinates at the beginning and end of said time, and count the pulse between them; then, from the abscissa and on the ordinates, to measure the height of the blood tension in millimetres—of course doubling the result, since the manometer consists of a tube, U-shaped, having two columns of mercury. When the tension was very uneven, I erected several ordinates, and then made an average of the different results.

Cat, curarized. *Cord cut* between the atlas and occiput (verified by post-mortem examination). Hemorrhage from the vertebral arteries checked by bovista. *All the cardiac nerves in the neck cut;* canula in right jugular; carotid used for observation. The sciatic nerve prepared. DuBois-Reymond's induction coil used for irritation. Tracheotomy; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
4:55:30	54	18
.0025 gramme strychnia injected.		
4:55:45	54	16
4:56:0	46	15
4:56:15	46	16
4:56:45	43	20
Irritation at 0 for 7″.		
4:57:0	43	22
4:57:15	43	27
4:57:30	43	27
4:58:0	40	25
Irritation at 0 for 15″.		
4:58:15	40	23
4:58:30	40	21
Observation suspended.		

Cat. Cord cut between the atlas and occiput (verified by post-mortem). Hemorrhage checked with bovista. *Vagi, sympathetics and depressors of Ludwig cut* in the neck. Sciatic prepared; curare; tracheotomy; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
4:56:0	53	58
.0025 gramme strychnia injected.		
4:56:15	53	58
4:56:30	47	64
4:56:45	48	90.5
4:57:0	48	114
4.57:15	47	111.5
4:57:30	46	97
4:58:15	45	77
4:59:0	44	70
5:1:30	50	78
5:2:30	52	81
5:3:30	52	81
.0025 gramme strychnia injected.		
5:4:15	53	84
5:4:30	54	88
5:4:45	46	79
5:5:45	43	70
5:6:45	45	62
5:7:15	46	62.5
.0025 gramme strychnia injected.		
5:7:30	45	65
5:7:45	46	70
5:9:15	41	64
5:9:45	41	62
5:11:0	41	56
5.13:45	43	55
5:14:45	48	63
5:25:30	46	56
Irritation of sciatic at 1 centimetre.		
5:25:45	45	56
5:26:0	43	57
5:26:45	43	54
Irritation at 0 for 5″.		
5:27:0	43	58
5:27:15	44	64
5:27:30	46	70
5:33:0	37	66
5:35:0	38	54
5:36:30	26	46
Irritation at 0 for 5″.		
5:36:45	29	56
5:37:0	29	50
5:41:15	31	48
5:42:0	32	48
5:43:0	23	48
5:44:0	23	46
.01 gramme strychnia injected.		
5:44:15	25	47
5:44:30	22	42
5:45:15	20	44
5:46:15	23	48
5:46:45	23	46
5:47:0	23	44
Observation suspended.		

Cat, curarized. *Cord cut* between atlas and occiput (verified by post-mortem). Bleeding checked by bovista. *All the cardiac nerves in the neck cut.* Canula in right jugular; carotid used for observation; sciatic prepared, etc.; tracheotomy; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
4:5:45	51	34
.0025 gramme strychnia injected.		
4:6:0	51	30
4:6:30	55	36
4:6:45	48	66
4:7:0	45	58
4:7:15	44	58
4:7:30	43	45
4:8:0	40	38
4:8:30	39	29
4:8:45	37	25
4 15:45	30	20
Sciatic irritated at 1 cent. for 29″.		
4:16:0	30	20
4:16:15	33	20
4:16:30	36	20
Observation suspended.		

Cat. All cardiac nerves in neck cut. Cord cut between the atlas and occiput (verified by post-mortem). Curare; artificial respiration; tracheotomy, etc.

TIME.	PULSE.	PRESSURE.
4:11:0	62	54
.001 gramme strychnia injected.		
4:11:15	59	54
4:11:30	55	54
4:14:48	45	22
.001 gramme strychnia injected.		
4:15:55	48	22
4:15:10	38	22
4:15:40	42	36
4:16:55	42	26
4:17:10	43	26
4:17:55	43	22
Observation suspended.		

Cat. Cord cut between atlas and occiput (verified by post-mortem). Hemorrhage staunched by bovista; canula in right jugular; carotid used for observation. *All cardiac nerves in the neck cut.* Sciatic nerve prepared; DuBois-Reymond's induction coil used for irritation; tracheotomy; artificial respiration, etc.

TIME.	PULSE.	PRESSURE.
4:20:15	42	44
.0025 gramme strychnia injected.		
4:20:30	42	45
4:20:45	41	47.5
4:21:15	39	44
4:21:45	38	35
4:22:0	38	32
4:22:45	37	29
4:23:0	37	30
Irritation at 0 for 15″.		
4:23:15	36	45.5
4:23:30	39	31
4:24:0	40	31
4:24:45	41	29
4:27:30	44	36
4:28:15	44	39
4:29:15	44	37
4:30:15	42	38
Irritation at 0 for 15″.		
4:30:30	44	38

TIME.	PULSE.	PRESSURE.
4:31:0	44	39.5
4:33:15	42	42
4:34:0	44	42
4:34:15	45	42
4:39:15	44	38
4:40:30	44	34
Irritation at 0 for 15″.		
4:41:0	44	38
Observation suspended.		

From the last series of experiments, and, indeed, from all others that I have related, I think we are warranted in concluding that Mayer was wrong in his theory that the slowing of the pulse is due to the presence of carbonic acid, irritating the roots of the inhibitory fibres of the vagi; and for this reason: In the experiments above narrated, I have invariably observed this slowing of the pulse, and yet, in all of them, I have used artificial respiration, by this means inducing a state of apnœa, and not allowing the carbonic acid to collect—nay, rather, causing an excess of oxygen.

But it will be seen at a glance that these experiments show more. They were also undertaken to prove or disprove the correctness of Schlesinger's theory. It will be remembered that Schlesinger said, that there exist in the cord vaso-motor centres for strychnia, which are habitually in a state of quietude; but that if the poison be administered, they are thrown into violent action. He said that, after cutting the cord, and severing all the cardiac nerves in the neck, if he administered strychnia and then applied a galvanic irritation to a sensory nerve, that he could obtain a higher rise of arterial pressure than he could if he administered strychnia, with all the animal's cardiac nerves and cord uninjured. I confess I cannot obtain identical results. I have a very marked rise on irritating a sensory nerve, but nothing to compare with what Schlesinger says he obtained. From my own experiments I am led to believe that he is right in his theory, and our results differ only in degree, not in kind. With all respect, I would venture to suggest that perhaps he did not have his cord entirely severed. If even a very few fibres are left, they are sufficient to convey the irritation to the medulla oblongata. I have had evident proof of this in many experiments. I have been almost certain that the cord was entirely severed, and have obtained the great rise that Schlesinger records, but on making an examination post-mortem, I have found some fibres still intact. Indeed it is by no means an easy surgical operation, working in the dark as one must, to strike the exact line between the atlas and the occiput, and then to make a clean cut of the whole cord and rapidly to insert the bovista, so that the animal may not lose any blood, so valuable here where a very severe shock has to be sustained by the animal; so that the most skillful operator will often fail in accomplishing his object, and need not blush at his failure either.

Dr. Carl Heinemann* has made some very interesting experiments on the influence of strychnia on the frog's heart. He concludes that the heart is slowed, and that the tetanus and the decrement of the pulse are mutually independent; also that the vagi are not paralyzed, since he could cause immediate diastolic arrest, by applying a galvanic stimulation. Mayer also found that the vagi are not paralyzed.

I now relate some of my own experiments on this subject, from which I conclude that the heart is slowed, and that the vagi are not paralyzed. My method consisted in raising the vagi on silk threads, and observing at what strength the induced current would slow the heart. Then I gave the poison. Now if the vagi are paralyzed, the same strength of current, or even the strongest current, should not have any effect on the heart beats; but, on the other hand, if they are not affected, the same phenomena should be presented as before giving the poison—that is to say, the same phenomena with regard to the cardiac pulsations. The current was prevented from spreading, by separating the nerves completely from any connection with the surrounding tissue.

Green Frog. Weight 90 grammes. Chest opened and vagi raised on silk thread. At 4:53 P. M., the heart beats 11 in 15 seconds. At 4:54 received .01 gramme strychnia injected into the abdomen. At 4:54:30 tetanus. At 4:56 heart beats 7 in 15 seconds. At 4:57, irritation of the right vagus slows the heart with DuBois' coil marking five centimetres. At 5:4 the heart beats 7 in 30 seconds. At 5:5 irritation at 5 centimetres slows the heart. At 5:12 the heart beats 4 in 30 seconds. At 5:13 irritation at 4 centimetres stops the heart. At 5:17, frog dead. At 5:19 the sciatic responds at 12 centimetres; at 5:25, thrusting probe down the spine elicits a marked response.

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* Beitrage zur Physiologie des Herzens. *Virchow's Archiv*, Bd. 33, pp. 394—410.

Green Frog. Weight 95 grammes. At 4:4 P. M., the heart was beating 15 times in 30 seconds. At 4:5, .005 gramme strychnia was injected into the abdomen. At 4:6:30, the heart beats 9 times in 30 seconds. At 4:8, the right vagus was irritated at 5 centimetres, DuBois' coil, and slowed the heart considerably. At 4:8:30, opisthotonos. At 4:9, .005 gramme of strychnia was injected into the abdomen. At 4:10, irritation of right vagus slows the heart. At 4:14, heart beats 4 in 30 seconds. At 4:16, irritation at 5 centimetres slows the heart. At 4:18, heart beats 4 in 30 seconds; at 4:19, irritation at 5 centimetres slows the heart one-half. At 4:26, heart beats 6 in one minute; irritation at 5 centimetres causes the heart to beat once in 15 seconds. At 5:2 heart beats 2 in 15 seconds; irritation at 5 centimetres makes the heart beat 2 in 20 seconds. At 5:22, all motion of heart and muscles had ceased. At 5:24 the sciatic nerve responds at 7.9 centimetres.

I made also some similar experiments on warm-blooded animals, one of which I now relate. The observations were made with Middledorpff's needle. This is a long slender silver needle which is thrust into the ventricle, using the walls of the thorax as a fulcrum. At each systole of the heart, of course the needle will move, and as it is of the nature of a lever of the first class, the movement of the heart will be greatly exaggerated, and may be counted with perfect ease.

Little Rabbit. Tracheotomy. Canula in jugular vein. Vagus prepared. DuBois' induction coil used for irritation. Middledorpff's needle thrust into the heart. At 5:34 P. M. the heart was slowed by irritating the vagus with the coil marking 10 centimetres. At 5:38, .005 gramme of strychnia was injected into the jugular vein. At 5:48, the heart was slowed by irritation of the vagus, with the coil at two centimetres. At 5:58, the same. At 5:59, the heart was considerably slowed by injecting .005 gramme of strychnia. The chest was now opened. At 6:00 the heart was slowed by irritation of the vagus, with the coil marking two centimetres. At 6:5 the same. At 6:40 the heart was slowed at one centimetre. Observation suspended.

In order to satisfy myself more fully of the correctness of my results, I performed what the Germans call Goltz's *Klopfversuch.* Of course the sensory nerves in and around the abdomen can convey an impression to the pneumogastrics; and if the nerves are not hampered in their action, they will reply by slowing the heart. I laid open the abdomen, and then by striking a sharp, moderately quick blow on its contents, I produced at times a slowing of the heart, and at times a complete stoppage of the pulsations of that organ, thus proving the correctness of my former observations, namely, that the pneumogastrics are not paralyzed by strychnia.

Green Frog. Weight 103 grammes. At 12:13 P. M., .005 grammes of strychnia was injected under the skin of the back. At 12:29 the heart beat 12 times in 30 seconds. The *Klopfversuch* was then performed. At 12:30, the heart beat nine times in 30 seconds. At 12:52, the heart beat nine times in 30 seconds; blow struck; at 12:53, heart beats five in 30 seconds. After death the sciatic nerve responds at 15 centimetres.

Dr. J. Steiner,* Assistant at the Physiological Institute at Halle, has also studied the action of strychnia on the frog's heart. He observed that when a one-third per cent. solution of the nitrate of strychnia was placed on the anterior side of the heart, the reduction of the heart beats was very small, but when placed on the posterior side of the heart the decrement was nearly one-half. He found the same result followed when he had previously given the frog atropia, inferring therefrom that the slowing was not due to irritation of the peripheral ends of the vagi. He then put the sinus venosus, separated from the action of the heart, into his solution of strychnia. In a short time it stopped, and was mechanically inexcitable. He then placed the auricles and ventricles, but without the sinus venosus, into the solution of strychnia, and found movements to continue for a long time; after they had stopped a mechanical irritation caused continuous beats for half an hour. He infers that the point of attack (*Angriffspunkt*) of strychnia is in the ganglia situated in the sinus venosus, and that it does not affect the ganglia in the septum or the auriculo-ventricular groove. I have repeated these experiments of Steiner in ten different instances, and have arrived at the same conclusion. In order not to anticipate my results, and to follow out a preconceived logical sequence, I refer to page 644, where an example of these experiments will be found detailed.

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* Zur Innervation des Froschherzens. *Reichert u. DuBois' Archiv*, 1874, No. 4, p. 474.

Let me now relate, in order, some of the experiments I have made on the influence of strychnia upon the cardio-nervous apparatus. These in number amount to twenty-four.

The action of strychnia is to slow the heart so palpably that I only relate one of my experiments in proof of this fact alone. Reference to very many other experiments, that were performed to prove other physiological phenomena, will give evidence of the same thing.

Frog. Weight 15 grammes. Sternum removed. At 4:31 P. M., heart beat 14 in 15 seconds. At 4:33, .005 gramme of strychnia was injected under the skin of the lower jaw. At 4:34 heart beat 2 in 15 seconds. At 4:35 heart beat 7 in 15 seconds. At 4:36. opisthotonos. At 4:37, heart beat 3 in 15 seconds. At 4:40 it beat 4 in 40 seconds. At 4:42, 4 in 15 seconds. At 4:48, 5:0, and 5:20 the same, and at 5:22 it beat 3 in 15 seconds, when the observation was suspended.

(It is to be noted that in all my experiments the heart has invariably stopped in diastole.)

Pursuing the same system as I had done before, I first endeavored to ascertain whether this pulse-slowing was due to a stimulation of the central ends of the vagi. I cut the said nerves on both sides, and after doing so I counted the heart beats; I then gave the poison and again counted the heart beats, and, as the following experiments show, observed a very decided slowing of the pulse; the heart appeared as if it was tired of beating, to use a familiar phrase; there never seemed to be a full energetic systole, and long diastolic pauses occurred. These results prove, then, that the phenomenon under consideration at present is not due to any hyper-excitability, or increased action of the central ends of the vagi.

Green Frog. Weight 140 grammes. Chest opened and both pneumogastrics cut. Heart beat 16 in 30 seconds. At 5:29 P. M., .01 gramme of strychnia was injected into the lungs. At 5:32, the heart beat 10 in 30 seconds. At 5:34 opisthotonos occurred. At 5:35 the heart beat 8 in 30 seconds. At 5:45 it beat 5 in 60 seconds; at 5:50, it beat 2 in 30 seconds; at 5:54, 3 in 60 seconds, and the observation was suspended.

Green Frog. Weight 142 grammes. Both pneumogastrics cut. Heart beat 12 in 15 seconds. At 4:40 P. M., .005 gramme of strychnia was injected into the lungs. At 4:44 tetanus. At 4:45, heart beat 5 in 15 seconds. At 4:48 the heart beat 6 in 30 seconds. At 4:49 opisthotonos. At 4:50 the heart beat 4 in 30 seconds; at 4:52 it beat 7 in 60 seconds; at 5:5 it beat 3 in 30 seconds and at 5:34, 4 in 60 seconds. Observation suspended.

Again, the pulse-slowing might be due to a stimulation of the peripheral ends of the pneumogastrics; for the purpose of determining this point, either positively or negatively, the annexed experiments were undertaken, with the effect of proving that the action of the poison is not located in this part of the cardio-nervous system. Here I paralyzed the peripheral ends of the vagi by the administration of atropia.

Large Green Frog. Weight about 150 grammes. Vagi paralyzed by atropia, as tested by strong currents (.01 gramme of atropia administered). At 11:50 A. M. the heart beat 14 in 30 seconds. At 11:51, .005 grammes of strychnia was injected. At 11:53, tetanus. At 11:54, heart beat 8 in 30 seconds; at 11:55, opisthotonos. At 11:56 heart beat 7 in 30 seconds. At 11:58, heart beat 5 in 30 seconds. At 12:03, heart beat 4 in 30 seconds. At 12:05, heart beat 3 in 30 seconds. At 12:07, heart beat 3 in 30 seconds. Observation suspended.

Green Frog atropinized; vagi tested as before. At 4:51, heart beat 13 times in 15 seconds. At 4:52, .0025 gramme of strychnia was injected into the abdomen. At 4:53, tetanus. At 4:55, heart beat 7 in 15 seconds; 4:57, heart beat 6 in 15 seconds; at 5:00, heart beat 3 in 15 seconds. Observation suspended.

To briefly recapitulate then, we have proved that strychnia slows the pulse; that this decrement is not due to any excitation of either the central or peripheral ends of the pneumogastrics; and we know it is not due to any action of the poison on the muscular structure. The inference then is that this phenomenon takes place through action on the cardiac nerve centres proper. This is proven positively by the experiments I now relate. These results also prove that the exact situation of these cardiac ganglia that are affected by the poison can be isolated to the sinus venosus, and that the centres situated in the auriculo-ventricular groove are not at all influenced by the drug.

Green Frog. Heart removed from the body, and the sinus from the ventricles, and observed.

I. At 4:48, heart beat 13 in 15 seconds. At 4:49, the sinus was placed in a solution of strychniæ acetas, at a temperature of 65° F., and the beats decreased to 7 in 15 seconds. At 5 P. M., the sinus beat 2 in 15 seconds. At 5:1:30, it had stopped beating and was mechanically unirritable.

II. At 4:49 the ventricles were placed in another dish containing strychnia of the same strength and temperature as in I. At 5:00, ventricles beat 10 in 15 seconds. At 5:1:30, ventricles beat 8 in 15 seconds. At 5:5, they beat 7 in 15 seconds. At 5:20, stopped beating, but mechanically irritable.

Frog. I. The sinus venosus was cut from the heart, and observed to beat 60 times a minute. At 12:24 P. M., it was laid in a solution of the acetate of strychnia. At 12:29 it beat 20 per minute, at 12:30 it beat 16 per minute. It could not be mechanically irritated to contract at 12:40.

II. At 12:24 the remainder of the heart was also laid in a solution of strychnia; it beat 28 per minute at 12:25, and 16 per minute at 12:29. At 12:40, it was mechanically irritable.

Large Frog. Heart removed. I. Sinus cut from the rest of the heart at 12:55 P. M., when it beat 52 per minute. At 12:56 it was placed in the solution of strychnia. At 12:57 it beat 48 per minute. At 12:59, it beat 44 per minute. At 1:0 it beat 32 per minute. At 1:4, it could not be mechanically irritated to contract.

II. At 12:56 the rest of the heart was placed in the strychnia solution; it beat very regularly for some time and then stopped. For a long time it could be excited to contract by mechanical stimulation.

It is to be remembered that in all my experiments under this head, of which the above serve as examples, that great care was taken in removing the heart itself, and the sinus removed from the rest of the heart; and also that the temperature of the strychnia solution was made exactly the same as that of the water from which the frogs had been taken.

I now propose to discuss what effect strychnia has on the nerves that govern the function of respiration.

In 1866 Leube* thought that perhaps the fatal effects of strychnia poisoning were produced by some action on the lungs, and that if an increased supply of oxygen was given to the animal, the working of the poison could be prevented. He concluded, from an elaborate series of experiments, that artificial respiration was very beneficial, and in some instances could save, even when the lethal dose was exceeded by three milligrammes. A little later, in 1868, Uspensky† confirmed Leube's results with especial reference to brucia. Rosenthal‡ followed, and agreed with Leube. In the year 1872, M. Brown-Séquard obtained the same results as Leube and Rosenthal, but explained the *modus operandi* differently. He thinks that the beneficial action ought to be ascribed to an irritation of the pulmonary branches of the pneumogastrics, thus exciting a reflex inhibitory action. Carbonic acid irritates these more powerfully than air, and thus has a more powerful inhibitory action. So he recommends the forcible inflation of carbonic acid. Its action is that of a simple irritant, and it produces or arrests convulsions, according to the part of the nervous system on which it acts.§ Dr. Rossbach ‖ was unable to obtain this effect on the strychnia convulsions, and, at his suggestion, Dr. Jochelsohn¶ began a series of experiments. His conclusions were, that in no case was it beneficial, and in some positively injurious. He says: "Die kunstliche Respiration weder einen Einfluss auf die erhaltung der Thiere, die mit Strychnin vergiftet sind, noch auf die Intensitaet und Dauer der Strychnin Kraempfe auszuueben im Stande ist, sondern das die Leben der Thiere nur um 3–4 Stunden verlaengern kann."*

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* *Archiv f. Anatomie, etc.*, s. 632, 1866.

† *Archiv f. Anatomie*, s. 523, 1868.

‡ *Archiv f. Anatomie*, s. 201, 1865.

§ *Arch. de Phys.*, 1872, p. 204, *et seq.*

‖ *Lond. Med. Record*, April 30, 1873.

¶ *Pharmakol. Untersuch.*, 1873, p. 93, *et seq.*

In January, 1874, Dr. Wilhelm Filehne† worked up this subject, and has given us a valuable paper. From numerous experiments of his own, and from those of all others except Jochelsohn, he assumes that artificial respiration has the power of arresting the convulsions, but seeks to find the *modus medendi.* He proves that Brown-Séquard and those of his school are wrong in supposing it to be due to any influence transmitted through the pneumogastrics, for he cut the latter nerves, and obtained the same results, or at least preserved the life of the animal for thirty-six hours. Doses that were lethal in animals with the vagi cut, were powerless in animals with the vagi intact, if artificial respiration was used. "When the period has come when the heart begins to tire, an important disturbance of the circulation begins. In vain a stronger and more energetic inflation (*Einblasung*) can only force a little blood to the breathing centre; the blood supply is not sufficient to affect the breathing centre—that is to say, to produce apnœa, and to strongly irritate the motor centre. The animal breathes spontaneously, becomes later tetanic, and finally dies through lameness of the heart's action."‡ M. Vulpian§ has no faith in the influence of artificial respiration. He apparently, however, bases his opinion on one experiment; at least he does not mention having made any more. He gave four milligrammes of strychnia, and applied artificial respiration in twelve minutes, and did not note any decrease in the number of spasms. The animal died in a couple of hours.

I will now relate the experiments I have made to determine the effect of strychnia on the nerves governing the respiratory movements. These were *fourteen* in number, and were performed on rabbits. The animal was simply tied in Czermak's rabbit-holder, tracheotomy performed. A T-shaped tube was introduced into the trachea, and a rubber tube then connected with this tracheal canula. On the distal end of the tube was placed a small, air-tight drum, connected on its upper surface with a long, light pen, after the manner of a lever of the first class. As the animal respired—by the contraction of the drum—the upper surface of the drum was drawn down, and the point of the pen was elevated, and the contrary, of course, took place when the animal made an expiration. The pen inscribed the result on Ludwig's registering apparatus.

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* *Loc. cit.* p. 96.

† *Archiv f. Anat.*, 1874, p. 361, *et seq.*

‡ *Loc. cit.* p. 373.

§ *Lecons sur l'appareil vaso-moteur*, a Vulpian, Paris, 1875, p. 689, *et seq.*

Rabbit. Left jugular prepared; tracheotomy. At 12:22:30 P. M. there were 11 respirations in 15 seconds. At 12:23:0, .0015 gramme of strychnia was injected toward the heart. At 12:23:15 there were 8 respirations in 15 seconds. At 12:26:30 there were 3 respirations in 15 seconds, and the same at 12:26:45. At 12:27:0 there were 6 respirations in 15 seconds, and at 12.27:15 tetanic struggles occurred, and the attempts at respiration were almost ineffectual. At 12:27:30 there were 7 respirations in 15 seconds. At 12:27:45 there were 6 respirations in 15 seconds. At 12:28:0 there were 5 respirations in 15 seconds. At 12:28:15 there were 4 respirations in 15 seconds. At 12:28:45 there were 4 respirations in 15 seconds. At 12:29:0 there were 5 respirations in 15 seconds. At 12·30:45 there were 3 respirations in 15 seconds. At 12:31:0 there were 6 respirations in 15 seconds. At 12:31:15 there were 5 respirations in 15 seconds. At 12:31:30 opisthotonos occurred, and for a period of 15 seconds no respiratory movements took place. At 12:32:0 there were two short inspirations, and then one expiration, and the animal was dead. The details of this experiment sufficiently illustrate all the rest of the series.

From these experiments it will be seen that the action of strychnia is to decrease the number of respiratory movements. My theory with regard to this result is, that at the very beginning the heart beats rapidly, and the respirations are accordingly quickened—that is, for the first few seconds only; but soon the heart loses its power by the action of the poison on the cardiac excito-motor ganglia, and consequently less blood flows to the respiratory centre, and, as a result, it does not fully perform its function, and the respirations are less frequent. When the respiratory centre becomes paralyzed, as it does later, or if enormous doses of the poison are given, then the phenomena of inspiration and expiration are stopped immediately. Of course this is only true where the dose has been toxic, but not lethal, or when artificial respiration has been employed; when the latter is not used, a large part of the effect is undoubtedly due to the tetanic contraction of the muscles of respiration. At every available lull in the spasms the animal appears to take in deep inspiration, thus seeming to desire to induce, by natural means, the condition we afterwards induced by artificial means, to-wit: a state of apnœa.

The objection may be urged that the slowing of the respirations is due to some action on the pneumogastrics. In order to meet this objection, I cut these nerves, and observed the same effect, as seen below. This might have been presupposed from our former conclusions as to the negative effect of the poison on the vagi, which we reached in our experiments as to the influence of the poison on the nerves governing the circulation.

Rabbit. Pneumogastrics cut; tracheotomy, etc. At 6:0:15 there were 18 respirations in 15 seconds; .00125 gramme strychnia was injected hypodermically. At 6:0:30 there were 14 respirations in 15 seconds. At 6.1:0 there were 13 respirations in 15 seconds. At 6:2:0 there were 15 respirations in 15 seconds; nystagmus very marked; pupil dilated. At 6:3:0 there were 14 respirations in 15 seconds. At 6:4:0 there were 16 respirations in 15 seconds. At 6:5:0 there were 15 respirations in 15 seconds. At 6:6:0 there were 16 respirations in 15 seconds. At 6:9:0 there were 16 respirations in 15 seconds. At 6:10:0 there were 14 respirations in 15 seconds. Observation suspended.

Having proceeded thus far in our experimentation, it is incumbent upon us to take up the consideration of the advantage or disadvantage of artificial respiration in saving the lives of animals poisoned with strychnia. Here, even more than anywhere else in our discussion, we have the two radical views presented to us; on the one hand Filehne asserting the wonderful power of artificial respiration in cases of strychnia poisoning, and, on the other hand, Jochelsohn's announcement that artificial respiration is perfectly useless, nay, indeed, injurious in such cases. In order to meet every point of dispute between these gentlemen, I obtained all my rabbits from the same stock, born and nourished in the same burrow, of nearly the same age and size, and, in a majority of cases, of the same litter. During our experiments they were all subjected to precisely the same influences, the same degree of heat and cold, the same food, etc. I never used an animal twice for experimentation. I first made myself thoroughly conversant with the different doses that were harmless, toxic and lethal in these rabbits, and then proceeded as narrated below.

Reference to page 631 will show by what means artificial respiration was maintained in these experiments.

I made *twelve* experiments to obtain these results, of which I narrate several.

Rabbit. Weight 1240 grammes. Tracheotomy. At 4:12 P. M., .00125 gramme of strychnia was injected hypodermically. At 4:14 convulsions occurred, and nystagmus was marked. At 4:20, opisthotonos did not again occur, but there were very violent convulsions. At 4:26 the severity of the convulsions decreased. At 4:34 the spasms became more intense. At 4:45 the convulsions had abated considerably. Artificial respiration was now stopped. Up to this time there were almost constant slight convulsive movements, but on stopping the artificial respiration, these stopped also, except occasional jerks on irritation. The animal now began voluntary respiratory movements; the respirations were quick, shallow and mostly diaphragmatic. At 5:6 there were only occasional contractions of single muscles. At 5:10 the respirations numbered 80 per minute. At 6:20 the breathing was regular and quiet, and assumed more of the costal type. At 10 A. M. the following day, the animal was quite lively, and ate voraciously.

Rabbit. Weight 1256 grammes. Tracheotomy. At 4 P. M. three (3) milligrammes of strychnia was injected hypodermically. At 4:1:30 tetanus. At 4:2 artificial respiration was begun. The convulsions now gradually lessened to a mere heightened excitability and tremulousness, except at 4:30, when they became again marked on irritation; occasional attacks of trismus also occurred. At 4:34 artificial respiration was suspended, and when the animal had recovered from its apnœa, it breathed voluntarily and regularly at the rate of 56 respirations per minute. At 4:45 the artificial respiration was renewed; at first it appeared to increase the excitability, but soon the animal became perfectly quiet. At 5 P. M. it was difficult to induce convulsions, even by strong mechanical irritation. At 5:15 tremulousness in the hind legs; no convulsions. At 5:40 the artificial respiration was permanently suspended, and the animal released; no convulsions occurred; the animal rose, ran around the room, and seemed quite lively.

Rabbit. Weight 1250.5 grammes. Tracheotomy. At 4 P. M. seven (7) milligrammes of strychnia was injected hypodermically. At 4:1:0 tetanus occurred, followed by opisthotonos. Artificial respiration was now applied. The violent convulsions still continued for a few minutes, but when a full state of apnœa was attained, they became intermittent, and only occurred occasionally. Almost continuous trismus was observed. At 4:11 a violent convulsion; at 4:14 another. At 4:26 they had subsided to mere tetanic jerks. At 4:30, on stopping the artificial respiration, as soon as the animal had come out of its state of apnœa, violent and continued convulsions occurred. The artificial respiration was renewed immediately. At 5:0 no convulsions occurred, unless excited by external violence. At 5:45 tries to get away. At 6:0 the spasms were few, and occurring at long intervals. At 6:2 artificial respiration was suspended; decreased amount of irritability; on recovering itself from apnœa, the animal made voluntary respirations at the rate of 52 per minute. At 6:5, artificial respiration being again renewed, the rabbit again became convulsed in a moderate degree. At 6:15 artificial respiration was suspended entirely, and with only a few slight twitches. At 9:00 P. M. the animal was still living, but died during the night.

Rabbit. Weight 1271 grammes. Tracheotomy. At 3:40

P. M. three (3) milligrammes of strychnia was injected hypodermically. At 3:45 opisthotonos. Artificial respiration was now begun. At 3:49 violent convulsions. At 3:56 continued trismus occurs. At 4:0 convulsive waves sweep over the whole body. At 4:15 the convulsions are not so grave; it is rather a continued trembling. At 4:50 the convulsions are slight. At 5:00 the animal is very quiet; no convulsions occur unless mechanically excited. At 5:15 spasmodic contractions of the several muscles occur. At 5:40 no more convulsions; the animal tries to get away. At 5:42 the artificial respiration was stopped, and, on voluntary respiration taking place, the number of movements was found to be 100 per minute. The artificial respiration was then renewed at 5:45, and continued till 6 P. M., when it was stopped permanently. After this stoppage, the animal evinced only a heightened reflex sensibility, by giving occasional slight jerks on irritation. It died the next day at 9 A. M.

Rabbit. Weight 1251 grammes. Tracheotomy. At 3:35 P. M., there was .002 gramme of strychnia injected hypodermically. Tetanic signs rapidly appearing, artificial respiration was immediately begun. At 3:38 slight tetanus. At 3:40 opisthotonos. At 3:50 long-continued, almost incessant, trismus was noted. At 4:15 only occasional convulsive spasms took place. At 4:30 artificial respiration was stopped, but as no voluntary respiration took place, it was renewed. At 5:00 the heart was beating very rapidly, and on the animal making one or two attempts at voluntary respiration, the artificial respiration was stopped.

Rabbit. Weight 1326.5 grammes. Tracheotomy. At 2:25 P. M., .0025 gramme of strychnia was injected subcutaneously. At 2:27 tetanus occurred. Artificial respiration was now applied. At 3:28 opisthotonos; nystagmus marked. Violent convulsions continued, and at 3 the animal was dead.

Rabbit. Weight 1269.5 grammes. Tracheotomy. At 3:42 P. M., .0025 gramme strychnia was injected hypodermically. At 3:42, on the appearance of tetanus, artificial respiration was begun. At 3:46, pleurosthotonos; this passed off and was followed by single spasms, following each other at not very long intervals. At 3:48, trismus was marked. At 3:52, alone remained. At 4, the artificial respiration was stopped and the animal lived for some time.

Rabbit. Weight 1315 grammes. At 3:28 P. M., .002 gramme strychnia was injected subcutaneously. At 3:30, tetanus occurred and artificial respiration was begun. At 3:35 a spasm occurred. At 3:36 convulsions occurred on the least irritation; the eyes were forcibly closed, the lids were raised with difficulty and nystagmus was extreme. At 3:44 excessive opisthotonos occurred. At 4:45, the animal was very quiet; at 5:13, the artificial respiration was stopped and voluntary, but quick respiratory movements ensued. A very slight spasm now occurred, and the artificial respiration was reapplied. Not a movement now occurred. At 5:25, the artificial respiration was permanently stopped and calm voluntary respirations took place, numbering 82 in the minute. The animal now lay perfectly quiet and did not even show heightened sensibility when touched. At 6, it was untied and presented no signs of tetanus whatever.

Now, I think these experiments plainly show that the middle way is not only safest, but also best. There can be no doubt that artificial respiration has a truly wonderful power in lessening the convulsions of strychnia-poisoning, and in prolonging the life of the animal, not for two or three hours, but for two or three days; and at the end of that time the animal may have died from other causes, tracheotomy for instance. Our own experiments will show, and any rational observer will acknowledge, that if you inject subcutaneously in a rabbit over two milligrammes of strychnia, the rabbit will rapidly die; now, by means of artificial respiration I have prolonged the life of the animal until the next day, nay far longer, and, what is more, the animal for many hours before its death has seemed very lively, eaten heartily, and not presented one sign of convulsions. Again, three milligrammes is an enormous dose of strychnia for a little rabbit, and should kill in a very few minutes, but by means of artificial respiration its life has been prolonged, not, as Jochelsohn says, for two or three hours, but for from twenty-four to thirty-six hours. Still further, a reference to the experiments before narrated, will show what truly frightful doses of the poison have been given and yet have not proved fatal; this can be explained no other way than through the influence of artificial respiration.

Now, on the other hand, I have never had an animal live over forty-eight hours after receiving two or three milligrammes of the poison, with two exceptions; and it is to be noted that if, during the later stages of the convulsions, I stopped the artificial respiration for a minute or two (not more) the animal would lie still, but on again joining the respiratory tube to the tracheal canula, quite violent convulsions would ensue, but these, in time, would pass off rapidly and leave the animal in its previous quiescent state. So I say, that in toxic and even lethal doses, artificial respiration is life-saving, and, that in large doses its power is great in postponing the fatal issue, and that, perhaps, in the cases where death has taken place, it has resulted from other causes, and not from the strychnia; but that it possesses the almost miraculous power ascribed to it by Filehne, of saving life in every case, and under all circumstances, is going farther, in my judgment, than the facts of the case will warrant.

Is this good influence of artificial respiration due reflexly to an irritation of the pneumogastrics, or to a super-oxygenation of the blood? The method I have employed in deciding this question, is to take two rabbits, equal in every respect, cut the pneumogastric nerves in both, and inject the same dose of strychnia in both; then to establish in one a state of apnœa through artificial respiration, and to leave the other to its own resources. Now this cuts off all influence of the pneumogastrics, and so both rabbits should stand an even chance of life, or rather, I should say, of death, if the artificial respiration exerts its influence through reflex stimulation of the pneumogastrics as Brown-Séquard thinks; but on the other hand, if it is due to super-oxygenation of the blood, the animal that has artificial respiration should be saved and the other should die. As the experiments narrated below show, this latter circumstance takes place, hence excluding Brown-Séquard's theory. It has been my experience, that even after the pneumogastrics are divided, a state of apnœa can easily be induced and voluntary respiratory movements stopped by artificial respiration, provided the insufflation be strong enough, and I cannot understand how it is possible that Brown-Séquard should state that such is not the case. Therefore it seems rational to me to suppose that the real and only influence of this artificial respiration is to keep the blood of the rabbit oxygenated, and the wheels of the animal economy in motion until the poison can be eliminated, which elimination takes place through the ordinary excretory channels, and not solely through the lungs.

(A.) *Rabbit.* Weight 1177 grammes. Both pneumogastrics divided at 10:12 A. M. At 10:15, .00125 gramme of strychnia was injected subcutaneously. At 10:24 tetanus. At 10:27, nystagmus marked. At 10:28 tetanus very pronounced. At 10:30, opisthotonos for fifteen seconds. At 10:33, opisthotonos for half a minute—death.

(B.) *Rabbit.* Weight 1165 grammes. Of the same stock, etc., as (A). Both pneumogastrics divided at 12:15 P. M. At 12:17, .00125 gramme of strychnia was injected hypodermically. At 12:19, artificial respiration was begun. At 12:22, heightened sensibility. At 12:24, tetanus. At 12:25, opisthotonos of short duration. At 12:26, nystagmus marked—violent convulsions now ensue. At 12:30, trismus was noted; convulsions have now almost entirely disappeared, except the trismus and a slight trembling of the thoracic muscles. At 1:5 general trembling; no marked convulsions appear. At 1:12 the trembling has disappeared except at the upper part of the sternum, and near the larynx. At 1:35, the animal was very quiet; not a sign of tetanus; at 1:45 it still remains quiet, and appears to attempt voluntary respiration. At 3, the heart is beating strongly and rapidly. At 3:5, the artificial respiration is stopped, the animal not showing signs of even heightened sensibility; the breathing is regular, and of course, slow, on account of the influence of the vagi being removed; the number of respirations is thirty-two per minute.

Having now examined the anatomical and physiological effects of strychnia on the brain, spinal cord and nerves, the question naturally arises: Has the time we have spent in these experiments been of any real practical value, and do our deductions show any results that will, in the future, lead to a more philosophical use of strychnia, or allow us to draw any parallel between its effects and the allied ones of traumatic tetanus, or the convulsions of epilepsy? This we will leave others to decide. It is necessary for us to know the effects our medicines are going to produce in disease, before we can conscientiously and willingly administer them. Empirical knowledge is good, and undoubtedly the foundation of our great science was laid in empiricism, in many instances; *a priori*, it is impossible to treat disease otherwise than empirically; yet it seems to me that we should use every means in our power to build up and adorn the lofty structure with all the details of philosophical research; provided, always, that such details be philosophic and yet practical. Unless we do this, as far as in us lies, we are, in a measure, looking through a glass darkly, and not face to face.

What conclusions are we, then, warranted in drawing in regard to the effects of strychnia?

1. Strychnia produces no appreciable primary lesion of the nerve substance proper; that secondary lesions are produced—granular disintegration—by the engorgement of the vascular system, and that this is more marked in the brain and cord than in the nerves.

2. That the convulsions of strychnia are not cerebral, and that they are much more severe after the ablation of the cerebrum, owing to the removal of Setschenow's ganglia.

3. Strychnia does not affect either the sensory or motor nerves at their periphery.

4. Both sensory and motor nerves, in their course, are unaffected by strychnia.

5. The tetanus-producing power of strychnia has its only action in the gray matter of the spinal cord.

6. In small doses, the primary action of strychnia is to excite the vaso-motor centre, causing thus a rise in the arterial pressure, and secondarily to paralyze this centre, and hence to supplement this rise by a fall.

7. In large doses, the vaso-motor centre is immediately paralyzed.

8. The slowing of the pulse, produced by the exhibition of strychnia to both warm and cold-blooded animals, is, in neither case, produced by any action on the central or per-

ipheral ends of the pneumogastrics; but, in warm-blooded animals, is due to action on the excito-motor ganglia of the heart, and in cold-blooded animals is due to action on the ganglia situated in the sinus venosus.

9. The main vaso-motor centre for strychnia is situated in the medulla oblongata, but simpler centres exist in the spinal cord.

10. The pneumogastric nerves are *not* paralyzed by strychnia, in either warm or cold-blooded animals.

11. Strychnia decreases the number of respiratory movements; at first from too little blood, and afterwards from too much blood flowing to the respiratory centres.

12. The decrease is not due to any action of the pneumogastrics.

13. Artificial respiration always moderates, and sometimes stops, the spasms; and this power is due to a maintenance of the oxygenation of the blood until the poison can be eliminated, and is not due to a reflex stimulation of the pneumogastrics.

ART. II.—THE DIAGNOSTIC SIGNIFICANCE OF THE TENDON REFLEX (KNEE PHENOMENON OF WESTPHAL).

BY H. M. BANNISTER, M. D., CHICAGO.

IN the *Archiv fuer Psychiatrie*, V., 1875, pages 492 and 802, Professors Erb and Westphal called attention to certain phenomena of contraction produced in muscles by percussion of their tendons, phenomena which, while some of them had long been matters of common observation, had received but little notice as regards their signification in health and disease. Erb found the patellar sinew reflex notably increased in several cases of spinal disease, *e. g.*, in three cases of compression of the cord, with or without myelitis, in consequence of decided spinal curvature; three cases of diffuse chronic myelitis, one of ataxia, etc. Westphal investigated the condition of